REMARKS

This is a full and timely response to the outstanding Final Office Action mailed January 29, 2009. Reconsideration and allowance of the application and presently pending claims, as amended, are respectfully requested.

Present Status of Patent Application

Upon entry of this Amendment, claims 1-48 are pending in the present application. Claims 29, 30, and 46-48 are withdrawn from consideration. Claims 1 and 31 are amended herein.

The prior art made of record has been considered, but is not believed to affect the patentability of the presently pending claims. Applicants believe that no new matter has been added and that a new search is not necessary.

Response to Applicants' Arguments

The Examiner stated in the Final Office Action at pp2-3 that:

> "With respect to assertion A, Applicants arguments are not found persuasive. components are distinct. But what does such a limitation mean? Distinct according to Claims 1 and 3 1 have been amended to make them recite the limitation that the the definition has a variety of meanings. The definition of 'distinct' is applied according to the definitions set forth by Dictionary.com (Exhibit **A).** Distinct means, 'not alike', 'dissimilar', or 'separate'. It is the opinion of the Examiner that the composition of Phillips teaches distinct components in all of these senses. In the sense that the components are 'not alike', Phillips obviates the instant claims. Each component has distinct properties. For examples, one PPI is released immediately, another PPI is enterically coated and slowly released, and there is a basic substance which is separate from both of the previous actives. Each of these components has a different physical property fiom the other. Thus, the populations of ingredients in the composition would necessarily be distinct according to this definition. In the sense that the components are 'separate', it is the position of the Examiner that Phillips meets this limitation too. While it may be true that components are admixed together, they still exist as 'separate' entities within the pharmaceutical mixture. Applicant is directed to Example VI of Phillips. Applicants arguments are not found persuasive."

Applicants have herein amended claims 1 and 31 to clearly state that **each** of the three (claim 1), or four (claim 31), components of the claimed compositions is **each** a population of beads, a population of pellets, a population of tablets, a population of granules, or a combination thereof. The amendments to the claims have been made for clarity. Accordingly, Applicants respectfully assert that the populations of pharmaceutical actives are clearly defined in the

amended claims submitted herein, and respectfully request that the Examiner's comments regarding such now be withdrawn.

Claim rejections under 35 U.S.C. §103(a)

Claims 1-28 and 31-45 were rejected under 35 USC §103(a) as being unpatentable over *Phillips* (US2002/0045646) and *Bergstrand* (US 5,817,338). The Examiner has asserted that the previous response to this rejection was unpersuasive.

Claim 1 and claims 2-28 dependent therefrom

In the Office Action, claims 1 to 28 and 31 to 45 were rejected under 35 USC § 103(a) as being unpatentable over *Phillips* (US2002/0045646) and *Bergstrand* (US 5,817,338). Applicants respectfully traverse this rejection.

Claim 1 is an independent claim. This claim is directed to an oral pharmaceutical composition comprising three populations of pharmaceutical actives provided in a capsule. Claim 1, as amended herein, clearly recites three populations, (i), (ii), and (iii), where each population is a population of beads, pellets, tablets, granules, ***or*** a combination thereof.

The populations are further clarified upon a reading of the specification, for example page 8, line 21 to page 9, line 11 which reads as follows:

> "The pharmaceutical capsule of the invention is made such that each population of beads, pellets, tablets or granules has a distinct physiological function.
>
> The function of the first population, comprising the pharmaceutically active substance, such as a proton pump inhibitor compound (PPI), that is rapidly releasable, is to deliver the pharmaceutical active beginning in the stomach. This is made possible due to the presence of an optional excipient and by the stable environment created by the elevated pH environment of the stomach brought about by the rapid disintegration and dissolution of the population of basic substance whose function is to rapidly deliver basic material to the stomach, which allows for precise control of the stomach pH to more than about 4.0 and less than about 7.0 and, typically, less than about pH 6.3. This pH can also be achieved in less than about 1 hour.
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> The function of the second population, comprising the pharmaceutical active substance, such as a proton pump inhibitor compound (PPI), that is released slower than that of the first population, is to deliver another quantity of the pharmaceutical active between the duodenum and just past the ileocecal junction. This is possible due to the presence of an excipient that controls the release of the pharmaceutical active and the choice and quantity of the basic substance delivered in the stomach by the population of basic substance. The

pharmaceutical active substance of the second population may be released in a delayed and/or sustained manner."

Even further examples of the description of the populations are provided in the specification, for example at page 11, lines 10 to 32 and throughout the Examples.

In contrast, neither *Phillips* nor *Bergstrand* teach or otherwise suggest a capsule comprising at least three populations where each population is a population of beads, pellets, tablets, granules or a combination thereof. In the Office Action mailed January 29, 2009, Example VI of *Phillips* is referenced by the Examiner. Example VI of *Phillips* discloses tablets that are compounded using known methods by forming an inner core of omeprazole powder mixed with sodium bicarbonate, and an outer core of omeprazole enteric-coated granules mixed with known binders and excipients. It is clear from *Phillips* that the described omeprazole powder and sodium bicarbonate form one (a **first**) distinct population. The omeprazole powder and sodium bicarbonate are uniformly mixed and, as described later in Example VI, the inner core is disbursed in the stomach where it is absorbed for immediate therapeutic effect, while the **second** population, the enteric-coated granules, are later absorbed in the duodenum. Thus, Example VI of *Phillips* pertains to a **single** population of granules, namely the enteric-coated granules, and clearly does ***not*** describe **three** populations, where each population is a population of beads, of pellets, of tablets, of granules, or a combination thereof, as recited in claim 1 of the present application.

The teaching or suggestion of **three** populations, wherein each population is a population of beads, of pellets, of tablets, of granules, or a combination thereof also cannot be found in *Bergstrand*. Furthermore, Applicants note that claim 1 recites a "capsule". ***Bergstrand clearly teaches away from the use of a capsule***. *Bergstrand* merely mentions capsule in the context of prior art and discusses the ***disadvantages*** of such a prior art capsule at column 2, lines 1 to 11. *Bergstrand* further uses pellets obtained from capsules in Reference Examples I and II, found at column 18. The disadvantages of the pellets obtained from capsules are shown in Table II at column 19. Specifically, Table II shows that pellets obtained from the capsules do not show good acid resistance when formulated in a tablet. The entire disclosure of *Bergstrand*, therefore, is directed to ***tablets*** and it ***teaches away from the use of capsules*** as claimed in the present application.

Applicants, therefore, assert that the cited references of *Phillips* and *Bergstand*, for at least the above reasons, do not teach, individually ***or in combination***, the encapsulated

formulations comprising three active substance populations as claimed in claim 1 as amended herein, and in claims 2-28 dependent therefrom. Applicants, therefore, respectfully request that this rejection under 35 USC §103(a) be withdrawn.

Applicants assert, therefore, that (i) the cited reference of *Bergstrand* specifically teaches away from the use of capsules such as those of *Phillips*; (ii) there is no statement or teaching in the *Phillips* reference that can provide any motivation for combining the compositions as described by *Phillips* with those as taught by *Bergstrand* to arrive at the compositions as claimed in the present application; (iii) the Examiner has failed to meet a *prima facie* case of obviousness by merely stating an assumption that one of ordinary skill in the art would be motivated to combine *Phillips* and *Bergstrand* without providing any explanation as to why.

In this regard, the MPEP section 2141 states:

> "The Supreme Court in KSR reaffirmed the familiar framework for determining obviousness as set forth in Graham v. John Deere Co. (383 U.S. 1, 148 USPQ 459 (1966))... As reiterated by the Supreme Court in KSR, the framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court are as follows:
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> (A) determining the scope and content of the prior art;
>
> (B) Ascertaining the differences between the claimed invention and the prior art; and
>
> (C) Resolving the level of ordinary skill in the pertinent art.
>
> In addition:
>
> When applying 35 U.S.C. 103, the following tenets of patent law must be adhered to:
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> (A) The claimed invention must be considered as a whole;
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> (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
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> (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention and
>
> (D) Reasonable expectation of success is the standard with which obviousness is determined.

Hodosh v. Block Drug Co., Inc., 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986)."

As reflected above, the foregoing approach to obviousness determinations was recently confirmed by the United Stated Supreme Court decision in KSR INTERNATIONAL CO. V. TELEFLEX INC. ET AL. 550 U.S. 1, 82 USPQ2d 1385, 1395-97 (2007), where the Court stated:

> "In Graham v. John Deere Co. of Kansas City, 383 U. S. 1 (1966), the Court set out a framework for applying the statutory language of §103, language itself based on the logic of the earlier decision in Hotchkiss v. Greenwood, 11 How. 248 (1851), and its progeny. See 383 U. S., at 15–17. The analysis is objective:
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> "Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or non-obviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." Id., at 17–18."

Indeed, as now expressly embodied in MPEP 2143, "[t]he ***key to supporting any rejection under 35 U.S.C. §103 is the clear articulation of the reason(s) why the claimed invention would have been obvious***. The Supreme Court in KSR noted that the analysis supporting a rejection under 35 U.S.C. §103 should be made explicit." (*Emphasis added, MPEP 2143*). "Objective evidence relevant to the issue of obviousness ***must*** be evaluated by Office personnel." (MPEP 2141). "The key to supporting any rejection under 35 U.S.C. §103 is the ***clear articulation of the reason(s)*** why the claimed invention would have been obvious. The Supreme Court in KSR noted that the analysis supporting a rejection under 35 U.S.C. §103 ***should be made explicit***. The Court quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that '[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." (MPEP 2141).

Applicants acknowledge that the reliance on an excessive number of references, by itself, may not weigh against the obviousness of the claimed invention. *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991). The same court espoused that "it is impermissible, however, simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps." Further, the "references themselves must provide some teaching whereby the applicant's

combination would have been obvious." Thus, without the indication provided by Applicants, "picking and choosing" components from a number of references merely to meet the present invention is substantially improper "hindsight".

The alleged rationale for combining the references is merely an improper ***conclusory*** statement that embodies clear and improper hindsight rationale, and still does not arrive at the combination of elements as claimed in the amended claims submitted herein.

Applicants, therefore, respectfully request that this rejection under 35 USC §103(a) be withdrawn.

Claim 31 and claims 32-45 dependent therefrom

In the Office Action, claims 1 to 28 and 31 to 45 were rejected under 35 USC § 103(a) as being unpatentable over *Phillips* (US2002/0045646) and *Bergstrand* (US 5,817,338). Applicants respectfully traverse this rejection.

Claim 31 is an independent claim. This claim is directed to an oral pharmaceutical composition comprising multiple populations provided in a capsule. Claim 31, as amended herein, clearly recites that the four populations (i), (ii), (iii), (iv), are each individually a population of beads, of pellets, of tablets, of granules, ***or*** a combination thereof.

The populations are further clarified upon a reading of the specification, for example page 8, line 21 to page 9, line 11 which reads as follows:

> "The pharmaceutical capsule of the invention is made such that each population of beads, pellets, tablets or granules has a distinct physiological function.
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junction. This is possible due to the presence of an excipient that controls the release of the pharmaceutical active and the choice and quantity of the basic substance delivered in the stomach by the population of basic substance. The pharmaceutical active substance of the second population may be released in a delayed and/or sustained manner."

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In contrast, neither *Phillips* nor *Bergstrand* teach or otherwise suggest a capsule comprising at least four populations, where each population is a population of beads, of pellets, of tablets, of granules, ***or*** a combination thereof. In the Office Action mailed January 29, 2009, Example VI of *Phillips* is referenced by the Examiner. Example VI of *Phillips* discloses tablets that are compounded using known methods by forming an inner core of omeprazole powder mixed with sodium bicarbonate, and an outer core of omeprazole enteric-coated granules mixed with known binders and excipients. It is clear from *Phillips* that the described omeprazole powder and sodium bicarbonate form one (a **first**) population. The omeprazole powder and sodium bicarbonate are uniformly mixed and, as described later in Example VI, the inner core is disbursed in the stomach where it is absorbed for immediate therapeutic effect, while the **second** population, the enteric-coated granules, are later absorbed in the duodenum. Thus, Example VI of *Phillips* pertains to a **single** population of granules, namely the enteric-coated granules, and clearly does ***not*** describe **four** populations each being a population of beads, of pellets, of tablets, of granules, ***or*** a combination thereof as recited in claim 31 of the present application, as herein amended.

The teaching or suggestion of four populations, where each population is of beads, of pellets, of tablets, of granules, ***or*** a combination thereof, also cannot be found in *Bergstrand.* Furthermore, Applicants note that claim 31 recites a "capsule". ***Bergstrand clearly teaches away from the use of a capsule***. *Bergstrand* merely mentions capsule in the context of prior art and discusses the ***disadvantages*** of such a prior art capsule at column 2, lines 1 to 11. *Bergstrand* further uses pellets obtained from capsules in Reference Examples I and II, found at column 18. The disadvantages of the pellets obtained from capsules are shown in Table II at column 19. Specifically, Table II shows that pellets obtained from the capsules do not show good acid resistance when formulated in a tablet. The entire disclosure of *Bergstrand*, therefore, is directed to ***tablets*** and it ***teaches away from the use of capsules*** as claimed in the present application.

Applicants, therefore, assert that the cited references of *Phillips* and *Bergstrand*, for at least the above reasons, do not teach, individually or in combination, the encapsulated formulations comprising four active substance populations as claimed in claim 31 as amended herein, and in claims 32-48 dependent therefrom. Applicants, therefore, respectfully request that this rejection under 35 USC §103(a) be withdrawn.

Applicants assert, therefore, that (i) the cited reference of *Bergstrand* specifically teaches away from the use of capsules such as those of *Phillips*; (ii) there is no statement or teaching in the *Phillips* reference that can provide any motivation for combining the compositions as described by *Phillips* with those as taught by *Bergstrand* to arrive at the compositions as claimed in the present application; (iii) the Examiner has failed to meet a *prima facie* case of obviousness by merely stating an assumption that one of ordinary skill in the art would be motivated to combine *Phillips* and *Bergstrand* without providing any explanation as to why.

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The alleged rationale for combining the references is merely an improper ***conclusory*** statement that embodies clear and improper hindsight rationale, and still does not arrive at the combination of elements as claimed in the amended claims submitted herein.

Applicants, therefore, respectfully request that this rejection under 35 USC §103(a) be withdrawn.

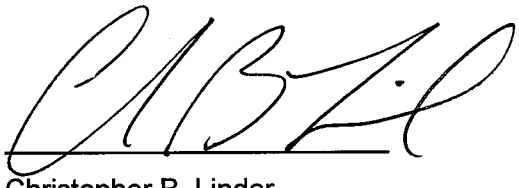
CONCLUSION

In light of the foregoing amendments and for at least the reasons set forth above, Applicants respectfully submit that all objections and/or rejections have been traversed, rendered moot, and/or accommodated, and that the now pending claims are in condition for allowance. Favorable reconsideration and allowance of the present application and all pending claims are hereby courteously requested.

Any other statements in the Office Action that are not explicitly addressed herein are not intended to be admitted. In addition, any and all findings of inherency are traversed as not having been shown to be necessarily present. Further, any and all findings of well-known art and official notice, or statements interpreted similarly, should not be considered well known for at least the specific and particular reason that the Office Action does not include specific factual findings predicated on sound technical and scientific reasoning to support such conclusions.

If, in the opinion of the Examiner, a telephone conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (770) 933-9500.

Respectfully submitted,



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